(FILE 'HOME' ENTERED AT 09:25:43 ON 13 AUG 2000)

FILE 'MEDLINE, EMBASE, CAPLUS, CANCERLIT, SCISEARCH, TOXLINE, BIOSIS'
ENTERED AT 09:27:53 ON 13 AUG 2000

L1	370415	S MN OR MN/CA9 OR MN/CAIX
L2	370415	S MN OR "MN/CA9" OR "MN/CAIX"
L3	397855	S CERVICAL OR CERVIX
L4	231	S L2 (30A) L3
L5	1495550	S ADENOCARCINOMA OR CARCINOMA
L6	69	S L4 (30A) L5
L7	23	DUP REM L6 (46 DUPLICATES REMOVED)
L8	1508	S HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION# OR (HSIL)
L9	1335	S LOW GRADE SQUAMOUS INTRAEPITHELIAL LESION# OR (LSIL)
L10	99	S L4 AND (L5 OR L8 OR L9)
L11	31	DUP REM L10 (68 DUPLICATES REMOVED)

L11 ANSWER 3 OF 31 MEDLINE DUPLICATE 1
AN 2000164359 MEDLINE
DN 20164359
TI Expression of **MN/CA9** protein in Papanicolaou smears containing atypical glandular cells of undetermined significance is a diagnostic biomarker of **cervical** dysplasia and neoplasia.
AU Liao S Y; Stanbridge E J
CS Department of Medicine, University of California-Irvine, Irvine, California; Department of Pathology, St. Joseph Hospital, Orange, CA, USA.
NC CA 19401 (NCI)
SO CANCER, (2000 Mar 1) 88 (5) 1108-21.
Journal code: CLZ. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 200006
EW 20000602
TI Expression of **MN/CA9** protein in Papanicolaou smears containing atypical glandular cells of undetermined significance is a diagnostic biomarker of **cervical** dysplasia and neoplasia.
AB BACKGROUND: Despite the enormous impact that Papanicolaou (Pap) smear screening has had on the incidence of cervical **carcinoma** in developed countries, there is still an unacceptably high frequency of occurrence of this cancer. In part, this is due. . . the Pap smears were decolorized and immunostained with monoclonal antibody to MN/CA9 antigen by the immunoperoxidase technique. The results of **MN/CA9** immunoreactivity were correlated with the histologic data in a semiblinded fashion. RESULTS: The follow-up biopsies showed that a high percentage (70%) of patients had low and high grade **cervical** intraepithelial neoplasia lesions, respectively (CIN I and CIN II or III).
Clinically significant lesions-**adenocarcinoma** in situ/**carcinoma** (AIS/CA) and CIN II or III-were found in 50% of the cases. Among these, 11% were AIS/CA. In the three. . . all cases of atypia showed positive immunostaining restricted to normal endocervical cells only. CONCLUSIONS: There is a clear association between **MN/CA9** immunostaining of atypical cells and the presence of significant lesions in the **cervix**. Similarly, there is a clear association between lack of expression of **MN/CA9** and the absence of **cervical** lesions. However, the screen does not allow discrimination between CIN I and atypia. The authors also found

L11 ANSWER 22 OF 31 CANCERLIT
AN 95607933 CANCERLIT
DN 95607933
TI Detection of **MN** in **cervical** biopsies by immunohistochemistry (Meeting abstract).
AU Chu C; Konrad K; Teramoto Y
CS Ciba Corning Diagnostics Corp., 1401 Harbor Bay Parkway, Alameda, CA 94502.
SO Proc Annu Meet Am Assoc Cancer Res, (1995). Vol. 36, pp. A153. ISSN: 0197-016X.
DT (MEETING ABSTRACTS)
FS ICDB
LA English
EM 199506
TI Detection of **MN** in **cervical** biopsies by immunohistochemistry (Meeting abstract).
AB . . . low grade diseases regress spontaneously, it would be useful to differentiate cases that will progress from those that will regress. **MN** is a potential marker for progressive dysplasia of the uterine **cervix**. **MN** expression has been linked to tumorigenicity in in vitro human and mouse systems. Immunochemical staining of **cervical** biopsies with a monoclonal antibody (M75) to the **MN** protein gave the following results: **LSIL**--20/46 (43%), **HSIL**--13/23 (56%), CIS--9/9 (100%) and squamous **carcinoma**-- 6/18 (89%) were positive for MN staining. This preliminary study indicated that MN expression was limited to a subset of.
. . positive cases increased with the grade of the disease. More studies utilizing cases with known clinical outcome will determine if **MN** expression is a marker for disease progression in dysplasias of the

study of a new ca[redacted]r-specific biomarker.

AB . . . the newly described endogenous MN gene th[redacted] is expressed in the tumorigenic phenotype of HeLa X fibroblast somatic cell hybrids. **MN** protein has carbonic anhydrase and putative DNA binding activity. With the exception of gastric mucosa, **MN** protein is expressed in neoplasia, particularly uterine **cervix carcinoma**, but not in benign tissue. This investigation; examined the pathogenetic and prognostic significance of **MN**-protein immunoreactivity in uterine **cervix carcinoma** with glandular differentiation. Paraffin sections from 77 **cervix** carcinomas with glandular differentiations including 36 pure adenocarcinomas and 41 adenosquamous carcinomas were immunostained with anti-**MN**-protein (M-75 monoclonal proprietary; Ciba Coming Diagnostics, Alameda, CA). A total of 64.9% of **cervix** carcinomas with glandular differentiation exhibit MN-protein immunoreactivity localized to plasma membranes, cytoplasm, and some nuclei of neoplastic cells only, but. . . did not help predict which patients would develop recurrence in the good prognosis groups. Our data, show that expression of **MN**-protein is associated with **cervix carcinoma** with glandular differentiation carcinogenesis. **MN**-protein immunolocalization may have a diagnostic role in confirming **cervix carcinoma** with glandular differentiation in histologically

L6 ANSWER 14 OF 31 MEDLINE DUPLICATE 10
AN 97334313 MEDLINE
DN 97334313
TI MN antigen expression in normal, preneoplastic, and neoplastic esophagus: a clinicopathological study of a new cancer-associated biomarker.
AU Turner J R; Odze R D; Crum C P; Resnick M B
CS Department of Pathology, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA 02115, USA.
SO HUMAN PATHOLOGY, (1997 Jun) 28 (6) 740-4.
Journal code: GEC. ISSN: 0046-8177.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199709
EW 19970902
AB Recently, a novel **tumor**-associated protein, termed **MN**, has been described in carcinomas of the uterine **cervix**, where its expression has been shown to be associated with malignant transformation. Because malignant transformation in the esophagus develops through a dysplasia-**carcinoma** sequence similar to that which occurs in the **cervix**, this study was performed to evaluate **MN** expression in normal, preneoplastic, and neoplastic tissues of the esophagus. Esophageal **tumor** resection specimens from 27 patients (12 squamous cell carcinomas, one multifocal squamous dysplasia, 10 Barrett's-associated adenocarcinomas, two Barrett's esophagus with dysplasia, two adenosquamous carcinomas) were immunohistochemically stained with a monoclonal antibody (clone M75) directed against the MN antigen. The localization of MN antigen, as well as the proportion of positively stained cells, were determined in sections of normal, dysplastic, and carcinomatous tissues. The staining characteristics were correlated with the pathological features of the tumors. Weak intracellular MN expression was detected only in the basal cells of normal squamous epithelium. However, inflamed and reactive squamous epithelium showed increased staining in the basal layer and in the overlying mature squamous cells. MN expression was significantly increased in dysplastic squamous epithelium ($P < .001$). All esophageal squamous cell carcinomas (100%) stained positively for MN antigen, where the pattern of staining was predominantly membranous. However, the degree of MN staining did not correlate with any of the pathological features of the tumors. In Barrett's epithelium, MN stained positively in all types of metaplastic cells and showed no difference in dysplastic epithelium. In contrast to squamous cell carcinomas, only 80% of esophageal adenocarcinomas were positive for MN, but the degree of MN expression was inversely correlated with histological tumor differentiation ($P < .015$). The results of this study suggest that (1) the tumor-associated MN antigen may play a role in proliferation and regeneration in esophageal squamous epithelium, and (2) loss of MN expression may be related to cancer progression in Barrett's-associated adenocarcinomas.
AB Recently, a novel **tumor**-associated protein, termed **MN**, has been described in carcinomas of the uterine **cervix**, where its expression has been shown to be associated with malignant transformation. Because malignant transformation in the esophagus develops through a dysplasia-**carcinoma** sequence similar to that which occurs in the **cervix**, this study was performed to evaluate

MN expression in n[redacted]al, preneoplastic, and neoplas[redacted] tissues of the esophagus. Esophageal tumor resection specimens [redacted]om 27 patients (12 squamous cell carcinomas, one multifocal squamous dysplasia, 10 Barrett's-associated adenocarcinomas, two Barrett's esophagus with.

L6 ANSWER 20 OF 31 MEDLINE DUPLICATE 15
AN 97102629 MEDLINE
DN 97102629
TI A study of biomarkers in **cervical carcinoma** and clinical correlation of the novel biomarker **MN**.
AU Brewer C A; Liao S Y; Wilczynski S P; Pastorekova S; Pastorek J; Zavada J;
Kurosaki T; Manetta A; Berman M L; DiSaia P J; Stanbridge E J
CS Department of Obstetrics and Gynecology, UCI Medical Center, University of
California, Irvine, Orange 92613-14091, USA.
NC CA 19401 (NCI)
SO GYNECOLOGIC ONCOLOGY, (1996 Dec) 63 (3) 337-44.
Journal code: FXC. ISSN: 0090-8258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
EW 19970301
AB The **MN** protein is a newly described biomarker found to be overexpressed in most **cervical** carcinomas. This study was an effort to evaluate the prognostic importance of **tumor MN** expression, HPV status, and the presence of other biomarkers in **cervical** cancers. **Tumor** DNA and protein for study were extracted from archived frozen tissue. **Tumor** tissues and controls were evaluated by Western blot analysis for **MN**, intestinal alkaline phosphatase (IAP), c-myc, and p53 protein overexpression. Immunohistochemistry was performed for **MN** quantification and the study of expression patterns in histologic subtypes of **cervical cancer**. HPV data were obtained by PCR amplification of extracted DNA using consensus and type-specific primers. Clinical data were obtained from the patients' records and from the **cancer** registry. Clinical and molecular data were correlated by chi2, Fisher's exact test, and logistic regression. The results demonstrate that IAP is not overexpressed in clinical specimens of cervical carcinoma, although in somatic cell hybrid experiments, overexpression of IAP correlates with the malignant state. None of 47 tumors, including those which were HPV negative, overexpressed p53. c-myc protein overexpression occurred in 11 of 52 tumors, most of which contained HPV 16, but this was not significantly different from the tumors as a whole. There was no apparent association between MN protein expression and the overexpression of c-myc protein. MN was overexpressed in all cancers and quantitatively varied with the histologic subtype. Specifically, lower expression of MN correlated with adenosquamous and less-differentiated histology ($P < 0.01$ for grade 3 tumors). Low expression of MN protein also correlated with HPV negativity ($P < 0.05$). In stage IB and IIA cancers, low expression of **MN** was associated with deeper cervical stromal invasion ($P < 0.03$). Further, low expression of **MN** correlated with lymph node metastases in small (<3.5 cm) IB and IIA **cervical** cancers ($P < 0.04$). These data suggest that **MN** is emerging as a potentially important new biomarker for **cervical carcinoma**. The overexpression commonly seen in **cervical cancer** is possibly associated with loss of a critical **tumor** suppressor gene located on chromosome 11. Low expression of **MN** antigen appears to correlate with several adverse prognostic features and further prospective study is warranted.

TI A study of biomark[redacted] in **cervical carcinoma** and clinical correlation of the novel biomarker **MN**.

AB The **MN** protein is a newly described biomarker found to be overexpressed in most **cervical** carcinomas. This study was an effort to evaluate the prognostic importance of **tumor MN** expression, HPV status, and the presence of other biomarkers in **cervical** cancers. **Tumor** DNA and protein for study were extracted from archived frozen tissue. **Tumor** tissues and controls were evaluated by Western blot analysis for **MN**, intestinal alkaline phosphatase (IAP), c-myc, and p53 protein overexpression. Immunohistochemistry was performed for **MN** quantification and the study of expression patterns in histologic subtypes of **cervical cancer**. HPV data were obtained by PCR amplification of extracted DNA using consensus and type-specific primers. Clinical data were obtained from the patients' records and from the **cancer** registry. Clinical and molecular data were correlated by chi2, Fisher's exact test, and logistic regression. The results demonstrate that IAP. . . of MN protein also correlated with HPV negativity ($P < 0.05$). In stage IB and IIA cancers, low expression of **MN** was associated with deeper cervical stromal invasion ($P < 0.03$). Further, low expression of **MN** correlated with lymph node metastases in small (<3.5 cm) IB and IIA **cervical** cancers ($P < 0.04$). These data suggest that **MN** is emerging as a potentially important new biomarker for **cervical carcinoma**. The overexpression commonly seen in **cervical cancer** is possibly associated with loss of a critical **tumor** suppressor gene located on chromosome 11. Low expression of **MN** antigen appears to correlate with several adverse prognostic features and further prospective study is warranted.

L6 ANSWER 21 OF 31 MEDLINE DUPLICATE 16
AN 96180293 MEDLINE
DN 96180293
TI Viral and histopathologic correlates of MN and MIB-1 expression in cervical intraepithelial neoplasia [see comments].
CM Comment in: Hum Pathol 1996 Mar;27(3):217-9
AU Resnick M; Lester S; Tate J E; Sheets E E; Sparks C; Crum C P
CS Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA.
SO HUMAN PATHOLOGY, (1996 Mar) 27 (3) 234-9.
Journal code: GEC. ISSN: 0046-8177.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199607
AB A recently studied **tumor** antigen, **MN**, has been associated with **cervical** carcinomas and **cervical** intraepithelial neoplasms (CIN), suggesting that it may serve as a marker for **cervical cancer** or **cancer** risk. To determine if expression of the **MN** antigen paralleled parameters reflecting viral or biological events in precursor epithelium, **MN** expression was correlated with MIB-1 expression, morphological phenotype, and human papillomavirus (HPV) distribution and type in a series of CINs. Seventy-three percent, 62% and 83% of CIN I, II, and III, respectively, were MN antigen positive. The proportion of neoplastic cells immunoreactive for MN did not correlate with the CIN grade or with HPV types stratified by their association with cancer. Evaluation of serial sections showed no correlation between the frequency of MN antigen staining, the proportion of MIB-1 immunoreactive cells, or the proportion of HPV positive cells detected by in situ hybridization (ISH). CINs associated with prototypical high risk (HPV 16) types exhibited increased immunostaining for the MIB-1 antigen and were more often classified as HSIL in contrast to the other types. Thus, although MN expression previously has been associated strongly with squamous carcinoma, it did not emerge as a specific marker for either cancer-associated HPV types or high grade CIN. CIN I lesions associated with low and high risk HPV types were not distinguished by MIB-1 expression and viral replication. This emphasizes the interrelationship between vegetative viral functions (including viral replication) and morphological phenotype, irrespective of HPV type.
AB A recently studied **tumor** antigen, **MN**, has been associated with **cervical** carcinomas and **cervical** intraepithelial neoplasms (CIN), suggesting that it may serve as a marker for **cervical cancer** or **cancer** risk. To determine if expression of the **MN** antigen paralleled parameters reflecting viral or biological events in precursor epithelium, **MN** expression was correlated with MIB-1 expression, morphological phenotype, and human papillomavirus (HPV) distribution and type in a series of CINs..

L6 ANSWER 24 OF 31 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 96054943 EMBASE
DN 1996054943
TI **MN** protein immunoloealization in uterine **cervix carcinoma** with glandular differentiation: A clinicopathologic study of a new **cancer**-specific biomarker.
AU Costa M.J.; Ndoye A.; Trelford J.D.
CS Department of Pathology, Univ. California-Davis Med. Center, 2315 Stockton Boulevard,Sacramento, CA 95817, United States
SO International Journal of Surgical Pathology, (1995) 3/2 (73-82). ISSN: 1066-8969 CODEN: IJSPFL
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology
016 Cancer
LA English
SL English
AB MN protein is the product of the newly described endogenous MN gene that is expressed in the tumorigenic phenotype of HeLa X fibroblast somatic cell hybrids. **MN** protein has carbonic anhydrase and putative DNA binding activity. With the exception of gastric mucosa, **MN** protein is expressed in neoplasia, particularly uterine **cervix carcinoma**, but not in benign tissue. This investigation; examined the pathogenetic and prognostic significance of **MN**-protein immunoreactivity in uterine **cervix carcinoma** with glandular differentiation. Paraffin sections from 77 **cervix** carcinomas with glandular differentiations including 36 pure adenocarcinomas and 41 adenosquamous carcinomas were immunostained with anti-**MN**-protein (M-75 monoclonal proprietary; Ciba Coming Diagnostics, Alameda, CA). A total of 64.9% of **cervix** carcinomas with glandular differentiation exhibit MN-protein immunoreactivity localized to plasma membranes, cytoplasm, and some nuclei of neoplastic cells only, but not in adjacent benign tissue. The MN-protein staining intensity and distribution was as follows: 37.7% strong diffuse (.gtoreq. 50% cells positive), 19.5% strong focal (< 50% cells positive), and weak (7.8%). Immunoreactivity occurred in both squamous and glandular areas of adenosquamous carcinomas and was unrelated to histopathologic features. Followup information was available on 67 patients: 31 exhibited recurrent disease (7 pelvic, 14 distant, and 10 both) at 1-144 months (mean 37: median 14), and 36 were disease-free at 12-216 months (mean 67, median 44.5). MN-protein immunoreactivity (all positives, both standard diffuse and strong focal, or standard diffuse only) exhibited no association with clinical outcome. Recurrent disease was associated with nuclear grade (P <.001), lymphatic invasion (P <.005), size on clinical examination or pathologic evaluation (P <.005), pelvic lymph node involvement (P <.05), and clinical stage (P <.05). MN-protein immunoreactivity did not correlate with these features and did not help predict which patients would develop recurrence in the good prognosis groups. Our data, show that expression of **MN**-protein is associated with **cervix carcinoma** with glandular differentiation carcinogenesis. **MN**-protein immunolocalization may have a diagnostic role in confirming **cervix carcinoma** with glandular differentiation in histologically challenging cases.
TI **MN** protein immunoloealization in uterine **cervix carcinoma** with glandular differentiation: A clinicopathologic